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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,174	01/25/2002	Robert E. Briggs	000295.00014	9144

22907 7590 10/22/2003

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	8

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,174	BRIGGS ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-41 and 66-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-41 and 66-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment submitted 5/12/03, Paper No. 7C is made. Claims 36-41 and 66-95 are currently pending.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 66-95 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 81-87, 91 and 95 are vague and indefinite because the claim 81 recites that a killed bacterium is administered to the ruminant. However, the live bacterium expresses a form of leukotoxin molecule which induces antibodies which neutralize biologically active leukotoxin. It is unclear how a killed bacterium will be able to express this leukotoxin which is the active portion of the vaccine. Accordingly, since these methods/vaccines/feed comprise killed bacteria the leukotoxin which is the active ingredient of the bacterium will not be expressed; therefore, it is unclear how the methods/vaccines/feed function. The claims do not require that the leukotoxin be present or expressed to the immune system of the ruminant. A vaccine comprising a killed

P.haemolytica containing the specified mutant gene, i.e., expresses a leukotoxin lacking amino acids 34 to 378, would appear to be analogous to a vaccine preparation comprising a killed wild-type *P.haemolytica,* which were well known in the art at the time the invention was made, since the killed vaccines would express no leukotoxin and it appears that they would produce the same immune response. Clarification is requested.

Claims 67-80, 90, 93 and 94 are vague and indefinite because it is unclear what is meant by administering a "lyophilized" (claim 67) versus a "lyophilized and reconstituted" (claim 74) *P.haemolytica* vaccine. Claim 67 recites the administration of a lyophilized bacterium. Is this lyophilized bacterium reconstituted or put in liquid in some manner in order to be active. Claim 74 specifically recites that the bacterium is reconstituted which makes it seem as if the lyophilized bacterium of claim 67 is not put in liquid prior to administration. It is unclear how this lyophilized bacterium would not degrade while sitting on animal feed. Claim 69 mentions top-dressing the feed of the ruminant; however, it is unclear that a dry powder of a lyophilized bacterium would allow for the active ingredient, the modified leukotoxin, to be expressed in the ruminant. Clarification is requested.

Additionally, claims 74, 90 and 94 recite that the *P.haemolytica* bacterium is reconstituted prior to administration. It is unclear whether this means that the lyophilized bacterium were put in growth media and grown prior to administration to the ruminants or if Applicants intend for this to mean the bacterium were placed in adjuvant and administered in

liquid form. What are the lyophilized bacterium being reconstituted in and how does this claim differ from claim 67, i.e, is claim 67 administered in dry form?

Response to Applicants' arguments:

Applicants argue that because no leukotoxin is to be produced after the bacteria are lyophilized or killed, the recited bacteria must produce the recited leukotoxin before they are lyophiled or killed or after reconstitution. These arguments are not commensurate in scope with the claimed invention. The instant claims do not recite that there is any leukotoxin present. Additionally, the instant specification fails to recite that the recited leukotoxin must be produced before the bacteria are lyophiled or killed or after reconstitution. Page 4, lines 10-18, mentions killed, lyophilized or killed and lyophilized bacterium, but no method steps are recited and there is no mention of killing or lyophilizing the bacteria after the leukotoxin is produced.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 67-87, 89-91 and 93-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "a method of inducing immunity to pneumonic pasteurellosis in a mammal comprising the steps of administering an isolated live *P.haemolytica* bacterium which expresses no biologically active leukotoxin, expresses a form of a leukotoxin molecule which is a deletion mutant of about 66kDa which lacks amino acids 34 to 378 and

which induces antibodies which specifically bind to and neutralize biologically active leukotoxin and contains no foreign DNA" and vaccines and feed comprising said live bacterium, does not reasonably provide enablement for "a method of inducing immunity to pneumonic pasteurellosis in a ruminant comprising the steps of administering an isolated live, or lyophilized or killed or lyophilized and reconstituted *P. haemolytica* which a) expresses no biologically active form of the virulence factor, b) expresses a form of leukotoxin which induces antibodies which neutralize biologically active leukotoxin; and c) contains no non *P.haemolytica* DNA", nor does it enable feed or vaccines comprising said killed, lyophilized, reconstituted and lyophilized bacterium." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 67-87, 89-91 and 93-95 are drawn to methods of inducing immunity to pneumonic pasteurellosis in a ruminant comprising the steps of administering an isolated live, or lyophilized or killed or lyophilized and reconstituted *P. haemolytica* which a) expresses no biologically active form of the virulence factor, b) expresses a form of leukotoxin which induces antibodies which neutralize biologically active leukotoxin; and c) contains no non *P.haemolytica* DNA and feed or vaccines comprising said killed, lyophilized, reconstituted and lyophilized bacterium. However, the instant specification only provides examples of vaccines, feed and methods which use a live bacterium, particularly the an isolated live *P.haemolytica* bacterium which expresses no biologically active leukotoxin, expresses a form of a leukotoxin molecule

which is a deletion mutant of about 66kDa which lacks amino acids 34 to 378 and which induces antibodies which specifically bind to and neutralize biologically active leukotoxin and contains no foreign DNA. The specification teaches that it is the mutant leukotoxin which is the active agent which specifically binds to and neutralizes biologically active leukotoxin. The specification solely provides immunization results using live recombinant *P.haemolytica* bacterium which expresses no biologically active leukotoxin, expresses a form of a leukotoxin molecule which is a deletion mutant of about 66kDa which lacks amino acids 34 to 378 and which induces antibodies which specifically bind to and neutralize biologically active leukotoxin and contains no foreign DNA. Results are also provided for this live recombinant bacterium top-dressed on feed. However, the specification provides no immunization or feed results using killed, lyophilized, or reconstituted and lyophilized bacterium. Additionally, no guidance is provided to explain what the bacterium is reconstituted in and whether it remains active and effective when administered to a ruminant.

In a killed or lyophilized and non-reconstituted bacterium, the mutant leukotoxin would not be expressed. Accordingly, it is unclear how these killed cells would have the ability to induce immunity to pneumonic pasteurellosis in ruminants. The specification provides no examples using the killed or lyophilized bacterium which are materially different than the live version of the bacterium. The results from the use of the live bacterium do not correlate to the killed bacterium because the active agent is not expressed in the killed bacterium. The vaccine art is highly unpredictable in the area of prevention of bacterial diseases. Since the specification

provides no results except for the use of an isolated live *P.haemolytica* bacterium which expresses no biologically active leukotoxin, expresses a form of a leukotoxin molecule which is a deletion mutant of about 66kDa which lacks amino acids 34 to 378 and which induces antibodies which specifically bind to and neutralize biologically active leukotoxin and contains no foreign DNA, or the isolated mutant leukotoxin molecule of 66kDa, lacking amino acids 34 to 378, claims 67-87, 89-91 and 93-95 are not enabled. Further, a vaccine comprising a killed *P.haemolytica* containing the specified mutant gene, i.e., expresses a leukotoxin lacking amino acids 34 to 378, would appear to be analogous to a vaccine preparation comprising a killed wild-type *P.haemolytica*, which were well known in the art at the time the invention was made, since the killed vaccines would express no leukotoxin and it appears that they would produce the same immune response.

The specification also fails to provide any method guidelines for administering a lyophilized bacterium to the ruminants. If the lyophilized bacterium is sitting on top of feed, how long will it last before it starts deteriorating? Will this lyophilized form allow for the leukotoxin to be presented to the immune system of the ruminant? There are no methods or experimentation results from immunization with a lyophilized bacterium provided in the specification. Additionally, there is no teaching of what the lyophilized bacterium is reconstituted in and no results demonstrating the lyophilized and reconstituted vaccine's efficacy. It is unclear that these lyophilized and/or lyophilized/reconstituted bacterium would work in the

same manner that a live recombinant bacterium would upon administration to a ruminant, i.e, grow and express the active leukotoxin portion.

Response to Applicants' arguments:

Applicants argue that because no leukotoxin is to be produced after the bacteria are lyophilized or killed, the recited bacteria must produce the recited leukotoxin before they are lyophiled or killed or after reconstitution. These arguments are not commensurate in scope with the claimed invention. The instant claims do not recite that there is any leukotoxin present. Additionally, the instant specification fails to recite that the recited leukotoxin must be produced before the bacteria are lyophiled or killed or after reconstitution. Page 4, lines 10-18, mentions killed, lyophilized or killed and lyophilized bacterium, but no method steps are recited and there is no mention of killing or lyophilizing the bacteria after the leukotoxin is produced.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 36-41 and 66-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. U. S. Patent No. 6,495,145. Although the conflicting claims are not identical, they are not patentably distinct from each other because the Patented claims are a genus which encompasses the instant claims, i.e, the patented claims do not specify whether the bacterium is live, lyophilized or killed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented..

7. Claims 36-41 and 66-95 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-29 of copending Application No. 09/736,169. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of 09/736,169 are a species encompassed within the genus of the instant claims. Although the method claims of Application No. 09/736,169 specify that the intended target of the method is a mammal wherein the instant claims recite a ruminant, since a ruminant is a mammal the scope of the claims is not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JGraser 10/21/03

JENNIFER E. GRASER
PRIMARY EXAMINER